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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,135	OKU ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14* is/are allowed.

6)☒ Claim(s) *1-8 and 10-12* is/are rejected.

7)☒ Claim(s) *13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 and 10-14 are pending in the application.

Rejections made in the previous Office Action which do not appear below have been overcome by Applicants amendment to the claims. Therefore, arguments pertaining to these rejections will not be addressed.

Information Disclosure Statement

The information disclosure statement filed June 30, 2004 and September 3, 2004 fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Additionally, the references were not supplied on a Form 1449 for consideration. It has been placed in the application file, but the information referred to therein has not been considered.

The indicated allowability of claims 1, 4, 6, 7 and 11-12 is withdrawn in view of the following rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating diseases/disorders such as diabetes, osteoporosis, hypertension, atherosclerosis, polycystic ovary syndrome, etc., does not reasonably provide enablement for the prophylaxis, or prevention, of all the diseases/disorders listed in claims 8 and 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, Applicants are claiming a pharmaceutical preparation (claim 8) for the prophylaxis or treatment of a number of diseases (e.g., diabetes, diabetic complications, polycystic ovary syndrome, skin disorders, etc.). Applicants also are claiming (claim 10) a method of preventing or treating a number of the same diseases.

The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The various diseases/disorders have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. For example, Applicants claims embrace a method of preventing or treating diabetic complications. The instant specification does not give any guidance as to the full range of diabetic complicating diseases that could be treated or prevented using the instant claimed process. In order to practice the claimed invention, one skilled in the art would have to speculate which diabetic complicating diseases/disorders could be prevented using the compounds found in the instant claims. The number of possible diabetic complicating diseases/disorders

embraced by the claims would impose undue experimentation on the skilled art worker. Applicants have not demonstrated that all of the diseases/disorders embraced by instant claims 8 and 10 could be prevented or treated. Therefore, based on the unpredictable nature of the invention, and the state of the prior art would prevent one skilled in the art from accepting any therapeutic regimen on its face.

Response to Arguments

Applicants' arguments filed August 4, 2004 have been fully considered. Applicants argue that: (1) the state of the prior art is continuing to seek advances in the treatment of the diseases named and pharmaceuticals containing a sulfonamide; (2) predictability is recognized by the U.S. Patent Office and cites a US Patent for support and other journal articles; (3) the direction or guidance is present and highlights page 21, paragraph at line 5; (4) there are numerous working examples in the instant specification such as Example 1 on pages 19-21;

(5) the breadth of the claims is limited to compounds that all have a sulfonamide group; (6) the various citations submitted established that the quantity of experimentation is known and acceptable in the art; and (7) the level of skill in the art is very high. Applicants conclude by arguing that all the diseases recited in method claim 10 are limited by the common thread "disease in a patient treatable with a pharmaceutical compounds having hypoglycemic activity".

In response, all of Applicants' arguments and various citations have been considered. The submitted citations were convincing in that most of the diseases listed in claims 8 and 10 are treatable. However, nothing in the instant specification or the various citations would lead one skilled in the art, based on the unpredictable nature of the invention, and the state of the prior art, that the instant claimed compounds and compositions would prevent every disease/disorder listed in instant claims 8 and 10. The various diseases/disorders have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. Therefore, the claims as such lack enablement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

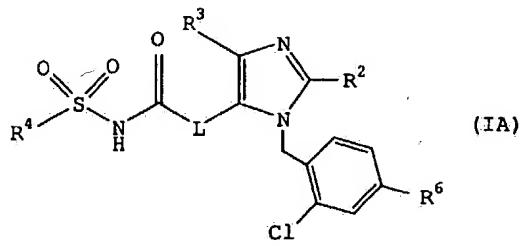
Claims 2, 3, and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 does not further limit claim 1 {see definition (10) under variable R^6}. Compounds 30 and 31 in claim 5 are not embraced by claim 1 (see the R^1 definition and the possible substituents).

Response to Arguments

Applicants' arguments filed August 4, 2004 have been fully considered. In regard to the rejection of the claims under 35 USC 112, second paragraph, Applicants argue claims 2 and 5 are within the scope

of instant claim 1 and points to Formula IA of claim 2, shown below, which appears on page 11 of the specification and specifically the R^6 variable.



(IA)

Applicants argue that the R^6 variable in Formula IA of instant claim 2 shows substitution of claimed substituents under the R^1 variable found in Formula (I) of instant claim 1.

In response, definition (10) under the R^6 variable in claim 2 is broader than the scope of substitution for the R^1 variable in claim 1 which is why claim 2 fails to further limit claim 1. As stated previously, nothing in the original filed claims or the instant specification would lead, suggest, or teach to one skilled in the art to substitute any of the claimed substituents of definitions (1)-(11), under R^1 in claim 1, on the "alkyl" portion of the "alkylaryl" (which is embraced by the definition of

"aryl") instead of the aryl portion of the "alkylaryl". It is also noted that in every other instance in the claims, Applicants were very specific about which substituents were optionally substituted with specific substituents {e.g., Claim 1, under the R^1 definition, definition (4), (7), etc.}.

The definitions of "alkyl" (page 4, lines 9-27), "aryl" (page 6, lines 34-38) and "alkyl-substituted aryl" (page 6, lines 39-40 and page 7, lines 1-6) have again been reviewed. See following each of these definitions that have been reproduced from the instant specification.

"Alkyl" and "alkyl moiety" are each preferably linear or branched alkyl. Preferable specific examples include methyl, ethyl, 1-propyl, i-propyl, 1-butyl, i-butyl, t-butyl, sec-butyl, 1-pentyl, i-pentyl, sec-pentyl, t-pentyl, methylbutyl, 1,1-dimethylpropyl, 1-hexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1-ethylbutyl, 2-ethylbutyl, 3-ethylbutyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1-ethyl-1-methylpropyl, 1-heptyl, 1-methylhexyl, 2-methylhexyl, 3-methylhexyl, 4-methylhexyl, 5-methylhexyl, 1-ethylpentyl, 2-ethylpentyl, 3-ethylpentyl, 4-ethylpentyl, 1,1-dimethylpentyl, 2,2-dimethylpentyl, 3,3-dimethylpentyl, 4,4-dimethylpentyl, 1-propylbutyl, 1-octyl, 1-methylheptyl, 2-methylheptyl, 3-methylheptyl, 4-methylheptyl, 5-methylheptyl, 6-methylheptyl, 1-ethylhexyl, 2-ethylhexyl, 3-ethylhexyl, 4-ethylhexyl, 5-ethylhexyl, 1,1-dimethylhexyl, 2,2-dimethylhexyl, 3,3-dimethylhexyl, 4,4-dimethylhexyl, 5,5-dimethylhexyl, 1-propylpentyl, 2-propylpentyl and the like.

Of these, particularly preferred is alkyl having 1 to 6 carbon atoms.

In the present specification, "aryl" and "aryl moiety" are each unsubstituted aryl or alkyl-substituted aryl. Examples of preferable unsubstituted aryl include C_6 - C_{10} aryl, such as phenyl, naphthyl and pentalenyl. Of these, preferred are phenyl and naphthyl.

"Alkyl-substituted aryl" means aryl substituted by at least one alkyl. The number of alkyl substituents is preferably 1 to 4.

> The aryl moiety of "alkyl-substituted aryl" is the same as for the aforementioned unsubstituted aryl, and the "alkyl moiety" is as defined above, which is preferably lower alkyl. Specific examples of preferable alkyl-substituted aryl include tolyl, xylyl, mesityl, ethylphenyl, propylphenyl and the like, with more preference given to p-tolyl.

The specification discloses that the alkyl can be linear or branched. The definition of alkyl does not state that the "alkyl" can be substituted. An example given for an "alkyl-substituted aryl" is a group such as *p*-tolyl (e.g., a phenyl ring substituted with an methyl group at the *para*-position of the phenyl ring). Again, note that in every other instance in the claims, Applicants were very specific about which substituents were optionally substituted with specific substituents {e.g., Claim 1, under the R^1 definition, definition (4), (7), etc.}.

Applicants argue that Formula (IA) under R^6 specifically names the substituents in question "halo" in substituent (4) and "aryloxy" in substituent (10). In response, substituent (4), which is "halo(lower)alkyl", under the definition of R^6 in claim 2 is not in question because R^1 in claim 1 states that the aryl can be substituted by

"(4) halo(lower)alkyl". However, in claim 2, R^6 representing definition (10), "lower alkyl optionally substituted by aryloxy" does not further limit claim 1 for reasons stated above.

Applicants argue that substitution is not dealt with on pages 9-10, as cited by the Examiner, but on pages 5-6 and generally on page 11, line 18. In response, all of these pages and lines have been reviewed. Paragraph bridging pages 5 and 6 teaches specifically "halo(lower)alkyl". Page 11, line 18 states "When the above-mentioned substituents are substituted" but only variable definitions such as R^4 state which substituents can be unsubstituted or substituted. Nothing in these pages would lead one skilled in the art to the R^6, in claim 2, representing definition (10), "lower alkyl optionally substituted by aryloxy"

Applicants argue that they should not be faulted for precisely defining what they intend by "aryl" and that their definition conforms to that which is standard in the chemical art. Applicants argue that claim 3 appears to be free of the stated criticism.

In response, Applicants' definition of "aryl" and "aryl moiety" being "unsubstituted aryl or alkyl-substituted aryl", which embraces substituents such as "phenyl" or "*p*-tolyl", is not being faulted. However, there is a problem with Applicants indicating that the "alkyl" portion (such as the methyl group in "*p*-tolyl") of the "alkyl-substituted aryl" is optionally substituted when the definition of "alkyl" in the instant specification does not indicate that the alkyl is unsubstituted or substituted. In regard to claim 3, claim 3 is dependent on claim 2 and is therefore, also rejected as being indefinite. For all the reasons given above, the rejection is deemed proper and is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619

(CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 and 10-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,242,474. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed invention is generically described in the patent. For example, see Compound 35 (see Figure 1, Sheet 1 of 3), the definition of an optionally substituted aromatic which includes substituents such as halogen in column 12, lines 55-67 and column 13, lines 1-3; and the various diseases/disorders in columns 18-19 which are embraced by the claims in the patent and the instant claims.

One skilled in the art would thus be motivated to prepare compounds embraced by the patent to arrive at the instant claimed invention with the expectation that the obtained products would be useful in treating diseases such as diabetes. Therefore, the instant claimed invention would have been obvious to one skilled in the art.

Allowable Subject Matter

Claim 14 is allowed over the prior art of record.

Claim 13 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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October 18, 2004

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